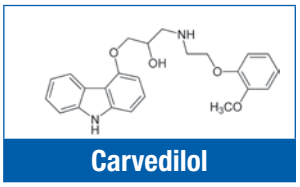
APPLICATION

Carvedilol and Related Substances

Ph. Eur. monograph 1745



Carvedilol

Overview

The Ph. Eur. Monograph 1745 outlines the separation of Carvedilol from impurities. This method was studied and improvements were made to provide faster separations within allowable adjustments.

Ph. Eur. Monograph 1745 Details

Reference Solution	**(b)** Dissolve 5 mg of Carvedilol Impurity C CRS* in 5.0 mL of the mobile phase and dilute to 100.0 mL with the mobile phase. Dilute 4.0 mL of the solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase. **(c)** Dissolve 5 mg of Carvedilol for system suitability CRS* (containing Impurities A and D) in the mobile phase and dilute to 50.0 mL with the mobile phase.

Column

Size	150 x 4.6 mm
Stationary Phase	End-capped octylsilyl silica gel for chromatography R (5 µm)
Temperature	55 °C
Mobile Phase	Dissolve 1.77 g of potassium dihydrogen phosphate R in water and dilute to 650 mL with the same solvent; adjust to pH 2.0 with phosphoric acid R and add 350 mL of acetonitrile R
Flow Rate	1.0 mL/min
Detection	Spectrophotometer @ 240 nm
Injection	20 µL
Run Time	6 times the retention time of Carvedilol

Relative Retention with Reference to Carvedilol (about 4 min)**

Impurity A	about 0.5
Impurity C	about 2.9
Impurity D	about 3.8

System Suitability

Reference Solution (b)	Minimum resolution of 3.5 between peaks due to Impuritiy A and Carvedilol

*Carvedilol Impurity C CRS (Y0000103) and Carvedilol for system suitability CRS (Y0001426) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

** Retention times, relative retentions, and retardation factors are provided for information only and are not mandatory, no deviation allowance is defined.

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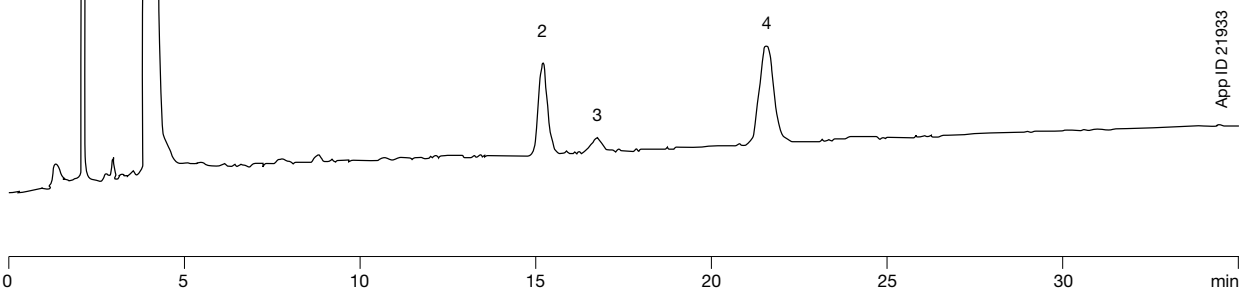
Method 1

Original Method as Described in the Monograph

Column: Kinetex® Core-Shell C8 5 µm
Dimensions: 150 x 4.6 mm
Part No.: 00F-4608-E0
Flow Rate: 1.0 mL/min
Sample: 1. Impurity A
2. Carvedilol
3. Impurity C
4. Impurity D
Elution Time of Last Peak: 21.53 min
Rs Impurity A and Carvedilol: 10.23



Adjustments for Meeting System Suitability
(European Pharmacopeia 9.0, Chapter 2.2.46. Chromatographic separation techniques)

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1
Mobile Phase pH	± 0.2 units	2.0 (as specified)
Concentration of Salts in Buffer	± 10 %	As specified in Monograph 1745 Details Table
Composition of the Mobile Phase	± 30 % of the minor solvent component relative or 2 % absolute, whichever is the larger. No other component is altered by more than 10 % absolute.	As specified in Monograph 1745 Details Table
Wavelength of Detector	No deviations permitted	240 nm (as specified)
Injection Volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory.	20 µL (as specified)
Column Temperature	± 10 °C	55 °C (as specified)
Stationary Phase	No change of the identity of the substituent permitted (e.g. no replacement of C8 by C18)	Octylsilyl silica gel for chromatography (as specified)
Column Length	± 70 %	150 mm (as specified)
Column Internal Diameter	± 25 %	4.6 mm (as specified)
Particle Size	-50 %	5 µm (as specified)
Flow Rate	± 50 %	1.0 mL/min (as specified)

Kinetex® Ordering Information

5 µm Minibore Columns (mm)					SecurityGuard™ ULTRA Cartridges‡
Phases	**30 x 2.1**	**50 x 2.1**	**100 x 2.1**	**150 x 2.1**	**3/pk**
C8	—	00B-4608-AN	00D-4608-AN	—	AJ0-8784 for 2.1 mm ID

5 µm MidBore™ Columns (mm)				SecurityGuard ULTRA Cartridges‡
Phases	**50 x 3.0**	**100 x 3.0**	**150 x 3.0**	**3/pk**
C8	00B-4608-Y0	00D-4608-Y0	—	AJ0-8777 for 3.0 mm ID

5 µm Analytical Columns (mm)					SecurityGuard ULTRA Cartridges‡
Phases	**50 x 4.6**	**100 x 4.6**	**150 x 4.6**	**250 x 4.6**	**3/pk**
C8	00B-4608-E0	00D-4608-E0	00F-4608-E0	00G-4608-E0	AJ0-8770 for 4.6 mm ID

‡SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

guarantee

If Phenomenex products in this technical note do not provide at least an equivalent separation as compared to a competing product of the same particle size, similiar phase and dimensions, return the product with comparative data within 45 days for a FULL REFUND.

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